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REPORT OF A CASE OF ERYTHROMELALGIA WITH THE POST-MORTEM FINDINGS.

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In an article appearing in the *Philadelphia Medical Times*[1], in 1872, Dr. S. Weir Mitchell first described a disorder, affecting chiefly the extremities, to which, in 1878,[2] he gave the name, erythromelalgia, or red neuralgia of the extremities. Particularly since the appearance of his second article, considerable interest has been manifested in the condition, and there are now on record in medical literature more than fifty cases, to all of which the name erythromelalgia has been applied. By Mitchell, the condition is considered a distinct disorder, but in some cases, particularly those described by Collier[3] in *The Lancet,* the symptoms seem to have arisen in the course of previously existing organic diseases, and there is some tendency at the present time to regard erythromelalgia as merely a symptom-complex.

In the articles by Mitchell which have appeared since the publication of his first contribution, and in reports by numerous other writers, the disease has been fully described from a clinical standpoint. There has, however, been no published case in which a post-mortem examination was made, if we except one reported by Auerbach,[4] in which only the spinal cord and some peripheral vessels and nerves were removed. The present case, therefore, derives its chief interest from the pathological examination which I was fortunate enough to be able to make. For most of the clinical material, I am indebted to Drs. R. E. Buchanan, of Independence, and G. W. Tapper, of Rowley, under whose care the patient came at different periods of his illness. The clinical record is as follows:

Family History.—The father is living and apparently healthy at sixty-eight years of age, but has had convulsions since he was a young man, and is doubtless epileptic. He does not appear to have suffered much mental deterioration. The mother is living at seventy-four, and she, with a sister and a half-brother of the patient, is in good physical health. A full brother died in middle life of some peculiar disease which was never positively diagnosed. The post-mortem examination in his case revealed only a condition of colitis.

Personal History.—At the time the erythromelalgia appeared, the patient was thirty-nine years of age. Previous to its onset, he does not seem to have had any severe illness. His early years were spent on a farm. In adult life he was an unusually vigorous man, being six feet in height and weighing about 200 pounds. After marriage, he became a commercial traveler; then a merchant in a small town, and finally, for about eight years preceding his illness, he was cashier in a bank. He took a prominent part in local affairs, carried considerable responsibility and was a busy man. His habits were unusually good, and no history of syphilis, gonorrhea or the use of alcoholic liquor could be obtained. He was the father of eight children, the last of whom was born two years after the beginning of his illness. This child, as well as the others, appears to be in normal mental and physical condition.

Present Illness.—In the fall of 1897, he had an attack of rather uncertain character. He first noticed a dull pain in the region of his stomach and liver, and this became so severe that he determined to consult Dr. Buchanan, who, on examination, found slight jaundice and some tenderness over the liver. Nothing else of importance was noted. He was confined to his bed for two weeks, but after this improved rapidly, and eventually went to work again in the bank. About the time of his return to work, he began to have a sensation of tingling and dull pain in the left index finger. I cannot learn whether the appearance of this symptom slightly preceded or followed his return to work. The pain was not nearly as severe as that which was present later in his feet, though it troubled him considerably. In three or four months it disappeared and did not recur until one week before his death. If any redness was present during this attack, it was not noticed. On the 5th of October, 1898, which was shortly after the disappearance of the pain in his hand, as he was walking home from his morning's work in the bank, he was suddenly seized with a very severe pain in his right great toe. He was able to continue his walk, though with much difficulty. The pain disappeared in about fifteen minutes, but, in a few hours, it returned, and henceforward was a very persistent symptom up to four months before his death. At first, no change was noted in the appearance of the skin of the affected toe, but later, a reddish discoloration always appeared with the onset of the pain. The condition spread rather slowly to the other toes of the right foot and finally included also the sole and the heel, all of which were the seat of exquisite pain at times. The instep was never as much affected as the other parts. When the right foot had become involved to this extent, the pain began to appear in the left foot, which by degrees passed through very much the same changes as the right had done. Shortly after both extremities had become affected, the middle toe of the right foot became very dark and ultimately gangrenous. The toe was moist, but there was never any line of demarcation. It was treated with antiseptic dressings for two or three weeks, but as there was no improvement, Dr. Buchanan amputated it close to the foot and the wound healed kindly. The toe was preserved for examination. Its gross appearance is as follows: The nail is gone, the epidermis is absent from the anterior end, and, on the second phalanx, is only loosely attached. The derma in these regions is black. The extreme tip of the toe is covered by a firmly attached, solid, black crust made up of skin and subcutaneous tissue.

Subsequently, the ends of all the other toes of both feet became very dark, almost black, but no gangrene supervened, and, after six weeks, this discoloration altogether disappeared. In June, 1899, which was after the amputation of his toe, the patient went to Chicago for consultation. He was there given a pair of shoes made so as to lessen the pressure on the ball of the foot. These seemed to give some relief for a time, but the general condition gradually grew worse. He next consulted a homeopathic physician, who advised him to remain in bed. He did so for two or three months, and, during this period, his pain was less than it had previously been. As soon as he got up, however, he found that he was worse than before. When in a sitting posture, with the feet raised, the latter were of a normal color and there was no disturbance of sensation except a deep-seated and constant, though not very severe, ache. As soon as he attempted to stand, however, the toes rapidly assumed a bright red color, which quickly spread to the ankle. In a short time, localized areas of dusky hue appeared, and these gradually became darker until they were deep purple or blue. The longer he stood, the more discolored all parts of the feet became, but certain islets were always darker than the intervening portions, and, as stated above, the arch was never so much affected as the other parts. With this change in color, there developed a most intense pain, which he described as like the sticking of many knives. It was so severe that he could not remain standing except for a very brief period, and at times he would cry out on account of his great suffering. Occasionally attacks came on without the feet being in a dependent position, but this was not common except at night, when he seemed to suffer considerably. There was intense pain in the gangrenous toe up to the time of its amputation, and no relief in other parts of the foot followed the operation. During an acute attack, there was very great tenderness to even the gentlest touch of the affected parts, but as soon as the pain was gone, he enjoyed having his feet vigorously rubbed, saying that this relieved the otherwise more or less constant ache. The nails were always tender and were particularly so when the toes were so dark. At this time, the nail from the toe, afterward amputated, and from one of the little toes, sloughed and the joints all became quite stiff. The great toes and those adjacent remained so, but the others returned to their former mobility as the discoloration disappeared. The local temperature was never much increased, and there was never much throbbing of the vessels, certainly nothing like Dr. Mitchell and others have described as being present in their cases. As the disease progressed, the spots of redness spread to the legs, but never went far above the knees except once, when, for a certain period, they extended up the inner side of the thigh to the perineum. Throughout this area, they came and went just as in the feet. In the spring of 1901, he complained one day of a pain over his heart, and his wife, upon examination, found there a bright red spot about the size of the end of a finger. She thought it was exactly like those on the feet. He had some pain in this region afterward, but the redness was not again present. Throughout the year 1900 and up to his death in 1901, he complained frequently of a dull, aching pain affecting all parts of his body. Rubbing benefited this to some extent.

Many different kinds of treatment were tried for the relief of his pain, but only one met with success worthy of note. Putting his feet in hot water almost always brought relief. When the pain was mild or only moderately severe, the relief was almost instantaneous, but, in a very severe attack, a short time elapsed before the pain ceased. Once, on going out into the snow, he thought the cold was of benefit, and on another occasion, when a physician evaporated some chloroform on one of the discolored spots, the pain was lessened. Nevertheless, he preferred the hot applications, but occasionally, when these were not quickly efficacious, he would alternate hot and cold applications, thinking that in this way he secured better results.

The patient's wife thinks that he had no impairment of sensibility for heat, cold or touch, and he certainly could judge very accurately the temperature of the water in which he placed his feet, it being necessary that this should be at a certain fixed point in order to bring relief. There was no tremor or spasm until near the end. No enlargement of the bones was noted, but no careful examination of these was made at any time.

In the spring of 1901, he began to cough and expectorate a great deal, and this continued more or less up to the time of his death. There was dullness in different parts of his lungs and rales were sometimes abundant. The attending physician diagnosed the condition as one of induration following pneumonia. At the same time, he complained a good deal of disturbance of vision. The eye-grounds, however, were not examined. He also had indigestion, from which he had not previously suffered. In June, he went to bed and did not get up again until Thanksgiving Day. During the early part of this period, he was troubled a great deal with nightmare. In August, dropsy appeared rather suddenly. The trunk, left hand, legs, feet and scrotum were all greatly swollen. The left side of the body was much worse than the right, the leg and foot on this side being almost three times their normal size. There was never any swelling in the right hand. For a period of two months, including the time when he was most ill, he sweated a great deal, but the perspiration was confined almost entirely to the right side of his body. On the days when he was worse, the perspiration was most free. Occasionally, this stopped abruptly at the median line; at other times, there was some moisture on the left side. His wife is quite positive as to this unilateral sweating, and says that not infrequently his night-shirt would be quite wet on the right side and dry on the left. At about this time, a mitral systolic murmur was first noticed, and an examination of the urine showed a large amount of albumin. He was also suffering severely from dull, heavy pains in the trunk and limbs. As he grew better, the sweating gradually ceased. While the edema persisted he was very ill, but, directly after its appearance, the acute pain in his feet and legs became very much less, and thereafter was not nearly so severe as it had previously been. In the fall he became very much better, and, on Thanksgiving Day, was allowed to sit up in a chair. His life had been despaired of several times during the summer, but he seemed so much better as cold weather came on, that his family even entertained hopes of his recovery. At this time the edema had almost or quite disappeared, and his urine contained only a trace of albumin. After Thanksgiving, he was dressed and able to be about each day, but he made no further progress. He had no particular pain, though in this respect he was a little worse than when in bed. He complained often of being very tired. This was his condition up to about the middle of December, 1901, when he again had severe pain in the left index finger, extending into the hand, with the same discoloration which had previously been present in his feet. On the 23d of the same month, while quietly sitting by the fire, he suddenly called to his wife that he could not see his hands. Almost immediately afterward he became unconscious. He straightened out in his chair, and a slight convulsive movement followed. In ten minutes the seizure was past, and he seemed as well as usual. He continued so until the 25th, when at eleven o'clock at night, he again became unconscious and had a convulsion similar to that on the 23d. These attacks continued to come on at intervals of every two or three hours until 8 p.m. of the 26th, when he died in a convulsion rather more severe than those preceding. He had been partially conscious in the intervals between his convulsions up to the time of his death, but, after the first seizure, he had frequent attacks of blindness.

Though he had been confined to bed almost the entire summer preceding his death, yet there was never any tendency to the formation of bedsores. After his first illness, no symptoms pointing to any disorder of the liver were noted. There was no great mental change at any time. He was occasionally much discouraged, greatly depressed and unusually nervous, but this was probably not more marked than would have been the case in any other illness equally severe and prolonged. There had been no ataxia and no headache. No curative treatment was of any avail, though he had been under the care of several regular physicians and also of homeopaths, eclectics, and osteopaths, besides trying a variety of patent preparations. While the hot applications had always been sufficient to control the pain, in June, preceding his death, he began to use morphine for insomnia. He voluntarily relinquished the use of this during the last month of his life.

The post-mortem examination was made seventeen hours after death. In the meantime arterial embalming had been done by an undertaker. I have not been able to learn the composition of the fluid used beyond that it contained arsenic, among other things. The embalming was very thoroughly done and doubtless produced a great change in the appearance of the tissues. It seemed also to interfere with their hardening and staining. The autopsy was made in a private house by Dr. George Boody, of Clarinda, and myself. The surroundings and the insufficient time at our disposal prevented us from making as thorough an examination as we would otherwise have done.

Anatomical Diagnosis.—Hypertrophy and dilatation of the heart; slight atheroma of the aorta and chronic valvular endocarditis; old double pleuritis; broncho-pneumonia; enlarged spleen; nephritis; passive congestion of liver; adherent dura; edema of pia-arachnoid.

The body is that of a male, six feet in height, well developed and fairly well nourished. The pupils are equal in size and both are dilated. The skin is pale and post-mortem lividity is slight. Rigor mortis, which is said to have set in early and to have been complete in two hours, is well marked in the feet, ankles and jaw, slight in the knees, hips and fingers, and almost absent in the elbows and neck. The muscles in the feet and calves of the legs are much atrophied, but equally so on the two sides. The arches of the feet are very high, but this condition is said to have been congenital. There is no edema and there are no areas of discoloration such as were present in life, the skin over the feet and legs being very pale. The third toe of the right foot has been amputated and a healthy scar marks the point of amputation. There is no scar on the penis. The panniculus adiposis is very slight over the chest and about 2 cm. in thickness over the abdomen. On opening the body, it is noted that the tissues, including the viscera, are unusually pale and firm, and that the vessels everywhere stand out prominently. These changes are doubtless due to the embalming fluid. The diaphragm is at the fifth interspace on each side. The lower margin of the right lobe of the liver is one finger breadth, and that of the left lobe two finger breadths, below the level of the umbilicus. The transverse colon is somewhat displaced downward by the liver.

Heart.—The apex is at the upper margin of the sixth rib and well outside the mid-clavicular line. The base is at the second interspace and the right border is one finger breadth to the right of the sternum. The pericardium is normal in appearance. The left side of the heart is firm and the right is moderately flabby. Mixed clots, which are quite brittle, project from the vessels and are present in the left ventricle and both auricles. The right ventricle contains an ante-mortem clot. The mitral orifice admits three fingers with difficulty and the tricuspid admits four. The left ventricular cavity is unusually large and its walls measure 2½ cm. at their thickest point. The anterior leaf of the mitral valve shows quite marked thickening and there is slight thickening along the free border of the posterior leaf. The tricuspid and pulmonary valves are about normal in appearance. The heart muscle appears to be quite healthy, except that on the inner surface of the left auricle and ventricle it is white and firm. The leaflets of the aortic valve are quite firm (doubtless due to the embalming fluid), but show no calcareous deposit. At the base of the aorta is an atheromatous patch, 1 cm. in diameter, elevated about 1 mm. above the surrounding surface; otherwise, the aorta presents a normal appearance. The walls of the coronary arteries seem to be a little thickened. Weight of heart 990 grams.

The lungs fill the chest cavity.

Left Lung.—The anterior portion of the upper lobe and the posterior portion of the lower lobe are adherent to the chest wall by some old fibrous bands. The lower lobe is also adherent to the diaphragm. The entire lung is firm. On section, it has a bleached appearance and no blood escapes except on deep pressure, when a frothy, somewhat blood-stained liquid runs out. The posterior portions of both lobes seem quite solid, though sections float in water. This partial consolidation is certainly ante-mortem. Weight 960 grams.

Right Lung.—The right lung is everywhere adherent to the chest wall, so that the pleural cavity is obliterated. The upper lobe presents a fairly normal appearance except for a moderate degree of thickening of the pleura beneath the adhesions. The middle and lower lobes are quite solid, but they are friable and are much torn on removal. Sections float in water. The pleura over these lobes is very greatly thickened.

Spleen.—The spleen is large and firm. The capsule is bluish in color and not much thickened. On the posterior border there is considerable post-mortem discoloration. At the lower end is a deep groove which nearly separates a portion of the spleen from the main body. Surface of section is mottled and shows very dark areas surrounded by larger pale red areas. The splenic pulp is firm. Weight 495 grams.

Adrenals.—The adrenals seem to be perfectly normal except for an unusual degree of hardness.

Left Kidney.—The left kidney is large and firm, and is surrounded by a considerable quantity of fat. The capsule strips readily, leaving a nodular surface with a number of small depressions. Some of the nodular areas are almost white; the intervening substance is pale gray. The cortex is gray in color and so far as can be determined, is of moderate thickness. Weight 250 grams.

Right Kidney.—The right kidney seems to be somewhat smaller than the left. The capsule is pale, and on the posterior surface is strongly adherent and portions of the cortex are removed with it. The surface of the kidney is nodular and much like that of the left. Weight 200 grams.

Liver.—The liver is unusually large. The capsule is transparent and glossy, and the liver substance shows through as a distinctly mottled mass, there being alternating large grayish and small dark areas. It is unusually firm and quite friable. Weight 2,475 grams.

Pancreas.—The pancreas seems to be normal.

Vermiform Appendix.—The appendix is 9 cm. in length, but shows nothing pathological.

Nothing unusual is noticed in the scalp, which is covered by a heavy growth of hair. The calvarium is moderately thick; diploe fairly well preserved. The dura is firmly adherent almost everywhere to the bone, and with difficulty separates from it. The pia-arachnoid is edematous and slightly opaque, the degree of opacity being nearly uniform for all portions. The vessels at the base are firm, but show no signs of calcareous degeneration or localized thickening of any kind. The convolutions are moderately plump, except in the frontal region, where there is slight atrophy. The cord and its membranes present a normal appearance.

Microscopic examination. Heart.—The muscle fibers appear to be increased in size. They stain well and the striation is well marked. In a very few there is a small amount of brown pigment near the poles of the nuclei. The blood vessels of the heart and other viscera will be described later under the general head of blood vessels.

Left lung.—The pleura is covered with a well marked exudate in which two distinct layers can be made out. The deeper layer is completely organized and contains many blood vessels and a considerable amount of black pigment. The superficial layer is fibrinous in character and shows here and there a trace of pigment. Everywhere throughout the section, there is a marked increase of fibrous tissue in the lung. The alveolar walls are much thickened and, in places, many of the air cells are partially or wholly obliterated. The majority of the air cells are empty, but some contain granular debris, while in others are fibrin, desquamated epithelium, some red blood corpuscles and a few large mononuclear cells with small nuclei. In parts of the section, a good many "Herzfehlerzellen," containing golden-brown highly refractive pigment are seen. The same pigment is found in less amount, mostly lying free, in the alveolar walls. Throughout the entire section the blood vessels are extraordinarily dilated, and are filled with red blood cells. In places where the alveolar walls are crowded together, the entire field consists of distended and tortuous vessels together with a small amount of supporting tissue.

Right lung.—The upper lobe shows the same condition of pleural thickening, increase of fibrous tissue within the lung and distention of the capillaries. There is less exudate into the alveoli, but "Herzfehlerzellen" are more abundant and show a well marked tendency to appear in clumps. In one area in the lower lobe, the alveoli contain abundant fibrinous exudate with many red blood cells, some exfoliated epithelium and much granular debris. In another area, extending from the pleura some distance into the lung, there is a much more marked fibrosis than in any of the other sections, and practically nothing is visible except bronchioles, fibroid tissue and greatly distended vessels.

Spleen and adrenal.—Beyond vessel changes, neither viscus shows any marked pathological change.

Left kidney.—The capsule is slightly thickened. Immediately beneath it, at irregular intervals, are seen clumps of round cells, mostly gathered about the stellate veins. These cells contain large nuclei with a relatively small amount of protoplasm. Some of the nuclei are vesicular, while others stain deeply. No lymphocytes are seen in these clumps, and only two polymorphonuclear leucocytes are found in an entire field. There is an increase of connective tissue everywhere, both in cortex and medulla, and there is also considerable parenchymatous change, though this is less noticeable than the interstitial. The capsules of the glomeruli are considerably thickened and frequently dilated, and many of the glomeruli have undergone a partial or complete hyaline degeneration, and some are replaced by masses of fibrous tissue. Frequently the tubules in the medulla, and, to a lesser degree, in the cortex contain hyaline material.

Liver.—Throughout the entire section studied there is marked dilatation of the intralobular veins and atrophy of the liver cells. Both of these conditions are slightly more marked at the center than at the periphery of the lobules. The central intralobular vein is in some instances so distended that its diameter is equal to a quarter of that of the whole lobule. Toward the center of some of the lobules the atrophy is so great that the columns of liver cells are represented only by homogenous, attenuated strings of tissue, in which an occasional nucleus may be seen. In some cases the cells are of about normal size, but all contain numerous fat droplets. Occasionally there is a small amount of round cell infiltration about an interlobular vein. No increase in fibrous tissue can be made out.

Pancreas.—Aside from the blood vessels, nothing of any importance is seen in the pancreas except a desquamation of the epithelium lining the walls of the ducts. In many places this is so marked that the epithelial cells entirely fill the lumen.

Muscle.—Sections of muscle from the first dorsal interosseous of the left foot and the left tibialis anticus show nothing abnormal.

Amputated toe.—The section for study is taken from the plantar surface at the proximal end of the distal phalanx. The epidermis and parts of the derma are necrotic. There is a well marked round cell infiltration of the derma and subcutaneous areolar tissue, particularly about the blood vessels, glands, ducts and nerves. Some of the vessels show a condition of suppurative arteritis, and many are plugged with thrombi.

Blood vessels.—In the amputated toe, the walls of the medium sized and small vessels, and even of the capillaries, are considerably thickened, but the thickening is almost altogether in the media, and the intima is but little affected. The lumen is only moderately decreased in size. In the large arteries, the middle and internal coats are both greatly thickened, and the lumen is relatively very small. In the largest artery in the section the internal coat is quite as thick as the middle, and the increase in both is such that only a small lumen is left, and even this is plugged with a thrombotic mass which has undergone partial organization. In this organizing tissue are several small openings in which a few red corpuscles are lying. Other large vessels, both arteries and veins, are plugged with thrombi, but in none is the thrombus so well organized as in the large vessel just mentioned.

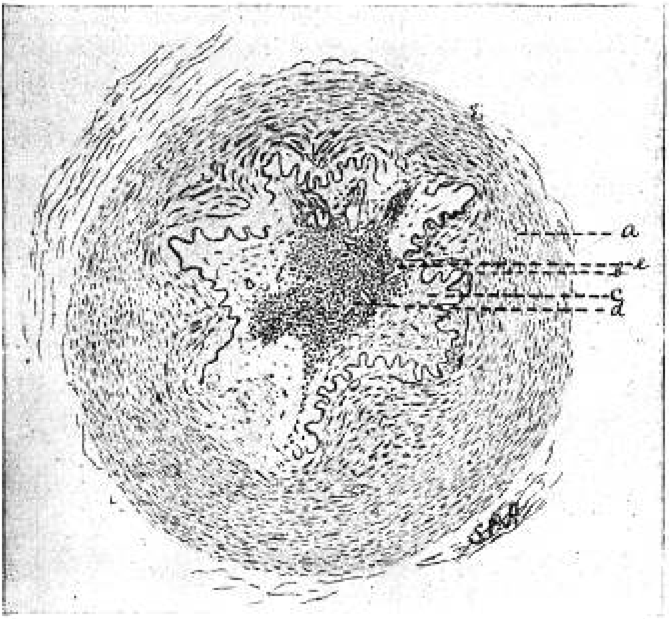

Fig. 1.—Left dorsalis hallucis artery. Eosin and methylene blue. (*a*) Muscular coat. (*b*) Elastic coat. (*c*) Intima. (*d*) Collection of round cells. (*e*) Small blood channels. For purposes of illustration the elastic coat is represented as darker than it really appeared.

When stained by Weigert's method, there seems to be considerable increase of elastic tissue in the arteries. The elastic layer lying between the middle and internal coats is often double, and there is some tendency to the formation of a new elastic layer on the inner surface of the intima.

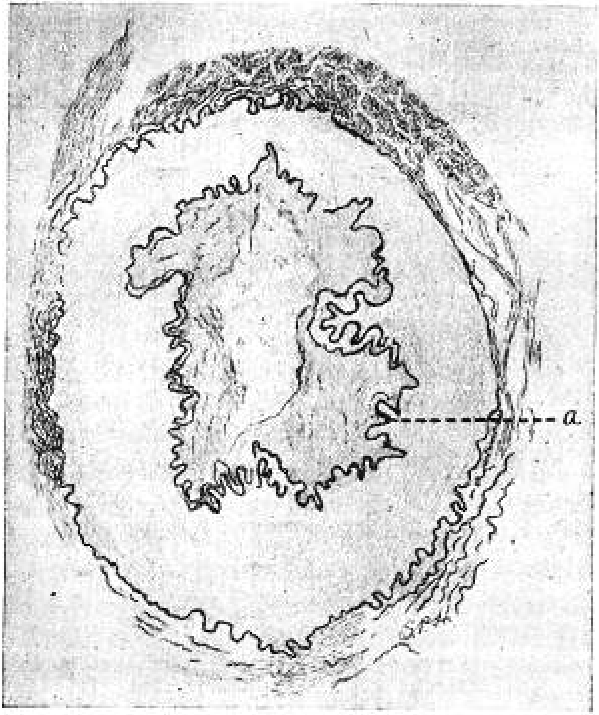

Fig. 2.—Left dorsalis hallucis artery. Weigert's elastic fiber stain. (*a*) Elastic coat.

The dorsalis hallucis artery of the left foot, removed at the time of autopsy, presents the most striking changes of any vessel seen. The muscular coat (a) is greatly thickened and unequally so, one side being almost twice as thick as the opposite. Inside the elastic coat (b) is a homogenous appearing material (c), with a few nuclei scattered through it. The center of the vessel is filled with a well marked accumulation of round cells (d), some with deeply staining and some with vesicular nuclei. In this collection of cells is a number of small openings (e), more or less filled with red corpuscles, and some lined with a distinct endothelial layer. The elastic tissue is increased in quantity and, under high power, is seen to be made up of three fairly distinct layers. Elsewhere in the interosseous muscle is seen a number of small and medium-sized arteries, all of which show well marked endarteritis, as well as increase of elastic tissue. In most cases the lumen is almost occluded.

The muscular coat of the right anterior tibial artery is slightly and irregularly thickened. The elastic tissue is somewhat increased and, at points, there is a moderate degree of endarteritis, which is unequally distributed. The right anterior tibial vein is normal in appearance.

In arteries of the pancreas (Fig. 3), there is a well marked increase of both intima (a) and media (b), though this is not quite so noticeable as is found in the vessels of the foot. The lack of uniformity, however, in the degree of thickening in the different vessels and in the different parts of the same vessel is greater than in any other tissues examined. The increase in elastic tissue is very noticeable. Some arteries are almost completely occluded, the lumen being represented only by a few small channels found in the center of the newly formed tissue. In the small arteries, the mesarteritis is much more marked than the endarteritis.

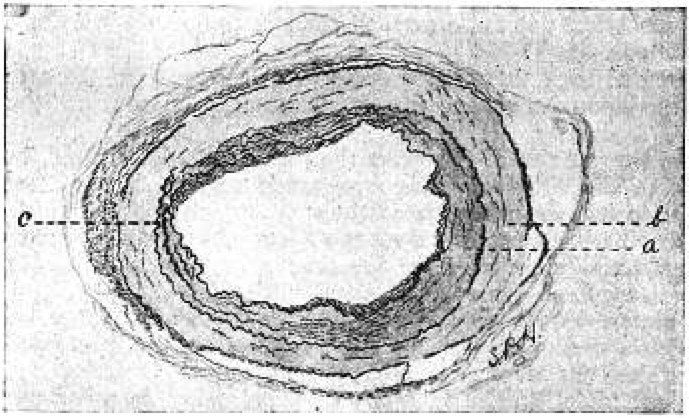

Fig. 3.—Small pancreatic artery. Weigert's elastic fiber stain. (*a*) Intima. (*b*) Media. (*c*) Elastic coat.

In the liver sections examined, only small vessels are seen. In one field nearly all these contain a great many leucocytes, though not enough to completely obstruct the vessels. They are mostly polymorphonuclear, but there are a few lymphocytes and an occasional large mononuclear leucocyte. There is no leucocytosis in the remainder of the section. The vessels all show slight increase of muscular and elastic tissue, but no endarteritis is seen.

The sections from the left kidney also include only small vessels, but in all of these, particularly in the cortex, there is a pronounced endarteritis and mesarteritis. In the cortex, the lumen of many of the vessels is almost occluded by the overgrowth of the intima, which is sometimes five or six times as thick as the muscular coat. In many of the vessels the muscular coat is degenerated, and does not take the stain well. The largest arteries show relatively less endarteritis than the others; but, on the contrary, they show greater increase of elastic tissue. The vessels in the medulla are much less altered than those in the cortex.

In the adrenal and spleen there is slight mesarteritis and endarteritis, but not more marked than is frequently seen in other conditions.

In the lungs there is no demonstrable disease of the arteries, but the blood vessels are greatly congested. There is no leucocytosis.

In the arteries of the heart the media is about normal, but in some of them the intima is moderately thickened. In a section taken to include a branch of the coronary artery a majority of the small vessels are found more or less completely plugged with leucocytes. In some of the vessels cut longitudinally the lumen is entirely filled for some distance with these leucocytes, which are almost invariably polymorphonuclear. In the large vessels there is also found a very great leucocytosis, but in most instances the white cells are scattered irregularly about. Occasionally they are found lying in the periphery of the stream. In other sections taken from the lower part of the wall of the left ventricle, a leucocytosis is also present, but it is less marked and the majority of the white cells are lymphocytes.

Sections from the basilar artery and the two internal carotids show no mesarteritis, but a moderate degree of endarteritis of irregular distribution. A piece of the aorta taken from the region of the atheromatous plaque shows, in addition to the ordinary appearance of atheroma, an increase of the elastic tissue. There is no endarteritis.

Nerves.—Portions of the anterior tibial nerve and its branches accompanying the dorsalis hallucis artery were preserved in formalin. The nerves of the amputated toe were also studied. The sections were stained according to the Weigert, Pal-Weigert and Van Gieson methods. The greatest change is found in the nerves of the foot. Here many of the fibers fail to take the characteristic stain, and there is considerable increase of connective tissue, both in the sheath and within the nerve bundles. In the nerves of the toe the same change is found, but to a less extent, and in the trunk of the anterior tibial nerve only a very small proportion of the fibers appears to be degenerated.

Posterior root ganglia.—The ganglia from the posterior roots of the fifth and twelfth dorsal nerves on the left side, and from the tenth dorsal nerve and an unnumbered lumbar nerve on the right side, were all preserved in Orth's fluid. The preparations obtained from these are not very satisfactory, but so far as can be determined, the cells are practically normal, and there is certainly no alteration of the nerve fibers.

Spinal cord.—The cord was preserved in formalin. At the end of eight weeks small pieces from each segment were placed in alcohol and cut and stained according to Nissl's and Van Gieson's methods. The remainder of the cord was placed in Müller's fluid, and later stained by the Weigert and Pal-Weigert methods. The Nissl preparations are not very good, but the cells appear to be normal. The nuclei are central and stain well. The chromophilic bodies are somewhat hazy, and there is a slight tendency to diffuse staining, but this is probably due to the imperfect method of fixation. Repeated examination of the pieces preserved in Müller's fluid fails to show any degeneration of the nerve fibers. The membranes of the cord are normal in appearance, and there is nowhere seen any leucocytosis or round cell infiltration. The arteries show slight thickening of intima and media.

Brain.—Macroscopic section of the brain fails to reveal anything abnormal.

In its clinical features, this case differs in a few particulars from the classical description of erythromelalgia given by S. Weir Mitchell. If we consider the patient's early illness, during which the symptoms pointed to disease of the liver, as a wholly independent affection, which it probably was, the signs of erythromelalgia were first noted in the left index finger, and their disappearance from this region in a few months, only to reappear after the lapse of three years, is interesting, and, as I think, unique.

In an article[5] contributed to the *Medical News* in 1893, Mitchell modified and made use of a table of Lannois in which the absence of gangrene is given as one feature which distinguishes erythromelalgia from Raynaud's disease, but there are now on record several cases, notably those of Sachs,[6] Elsner,[7] Rost[8] and Dehio,[9] in which gangrene developed, and even in one of S. Weir Mitchell's later cases[10] it came on, though only after an operation for nerve stretching and section. The occurrence of gangrene in my case, therefore, cannot be considered of any great interest.

In most of the cases so far reported it is distinctly stated that cold relieved, while heat aggravated the pain. The only exceptions to this that I can find are the cases of Eulenberg,[11] where the pains were worse in winter than in summer; of Bernhardt,[12] where the pains were worse in windy weather, and were increased by cold; and of Auerbach[4] (Case IV.), where cold at first brought relief, but later cold and heat were used alternately. In my patient, cold relieved the pain somewhat, but was never so efficacious as warmth.

Though the microscopical studies so far have almost invariably revealed marked arterial disease, yet clinical records of such changes are infrequent. In many of the reports nothing whatever is said of the condition of the heart and blood vessels, and, considering how carefully other phases of these cases were studied, it is probable that the findings in this respect were negative, and in some instances it is stated that they were negative. Out of considerably over fifty cases I could find only the following in which well marked disease of the vascular system was noted. S. Weir Mitchell[5] in one instance reports a systolic murmur, but makes no mention of enlargement of the heart or of change in the arteries. Again, in a man of sixty-one, he and Spiller[13] found a faint rythmic murmur at the apex, but say that the arteries were soft and of normal tension. Gerhardt's[4] patient had palpitation and a weak pulse, and in Dehio's[9] patient the radial impulse in the affected arm was weaker than in the other, but there was no striking rigidity of the vessels, and in neither case was there any change noted in the internal organs. In Henoch's[15] case there were angina pectoris and other signs of arteriosclerosis. Saville[16] speaks of his patient as having a heart which was "nervous," but structurally sound, and, though the radial arteries were a trifle thickened, there was no definite arterial lesion. Elsner[7] found far-reaching arteriosclerosis and slight hypertrophy of the left ventricle in one instance, but this was in a man of sixty-four who had previously had syphilis. In one of Sachs'[6] patients there was a faint change in the first sound at the apex of the heart, but the pulse was strong and regular and there was no evidence of arterio-sclerosis. In another patient he found marked dilatation of the heart and a widespread arteriosclerosis. In my case there is no clinical record of arterial disease, and at the autopsy it was impossible, on account of the embalming, to determine by palpation, the condition of the vessel walls. The enlargement of the heart found post-mortem, however, was so great that it must have produced well marked clinical signs, and the fact that such a condition has not been observed in the cases of Elsner and Sachs would seem to show that marked cardiac hypertrophy or dilatation is not a common accompaniment of erythromelalgia.

The edema which came on in August, 1901, with the succeeding disturbances of vision, gastric distress, unconsciousness, convulsions and death, were all probably directly dependent on a chronic nephritis. It is difficult to explain the unilateral sweating and edema. The right hand, which was always free from the erythromelalgic process, was, of all the extremities, the most free from edema; but the right foot, which was less affected by the edema than the left, was the seat of erythromelalgia before the left foot had become involved, and it was possibly, throughout, the seat of a little greater pain than the other. It is well known that in uremia there is at times a great increase of activity in the sweat glands, and the sweating of the right side may readily account for the relative lack of accumulation of fluid there. The question still remains, however, as to why the sweating should have been greater on the one side than on the other. There was nothing in the case to lead to the belief that the hemidrosis was hysterical. In Henoch's[15] patient, there was unilateral sweating, and, in a number of instances, there has been sweating of the affected part, especially when this was the seat of acute pain. In one of Mitchell's[17] patients, there was, at one time, edema from the waist down. In the present case it is unlikely that the appearance of the edema had anything to do with the partial disappearance of the pain. I think it more probable that it was a mere coincidence, and the fact that the pain did not return after the edema had disappeared seems to lend countenance to this view.

Up to the present time the amount of tissue available for examination has been strangely meager. In Woodnut's[18] case, where a toe had been amputated, the surgeon described it as follows: "The amputated part had turned to gristle, and had no circulation." In Dehio's[9] patient, who had had erythromelalgia for four years in the left hand and foot, 4 cm. of the left ulnar nerve and artery were removed and sectioned. The nerve was found to be normal, but in the artery there was marked endarteritis, with a diminution of the lumen to one-half its former size. The adventitia was normal and the media practically so. Elsner's[7] second patient, a woman of forty-two, had suffered for twenty years with erythromelalgia of the left index finger. This was amputated, and the following pathological report on the amputated tissue was made by Dr. Steensland: "There is occasional slight thickening of the intima of both the large and small arteries. About the small arteries are occasional foci, with infiltration of lymphoid cells. Veins are apparently normal.****Careful examination of the nerves, Pacinian corpuscles, sweat glands, hair follicles and muscles showed nothing aparently abnormal."

Dr. Mitchell's two cases, from which pathological material was obtained, and also the case which he and Dr. Spiller together reported, are as follows:

Case I[5]. Male; age twenty-one; had sustained a severe injury of the right foot, and, almost immediately afterward, erythromelalgia of this member developed. Fourteen months later, at Dr. Mitchell's suggestion, Dr. Keen exsected two and one-half inches of the musculo-cutaneous nerve, and the same length of two branches of the internal saphenous. On examination, these nerves were found to be normal. Cultures from the blood and nerves also yielded negative results.

Case II[10]. Male; age forty-eight; erythromelalgia of the right foot had been present for eight months. At Dr. Mitchell's request, Dr. T. G. Morton excised portions of the musculo-cutaneous and internal saphenous nerves which, when examined, were found to be normal. On the fifth day, signs of gangrene appearing in the foot, the friends became dissatisfied and removed the patient to another hospital, where, one week later, he died during an attempted high amputation. It was reported to Dr. Mitchell that the vessels of the amputated limb, even the smallest arterioles in the sole of the foot, showed thickening of the muscular coat, while in the larger vessels there were calcareous deposits.

Case III[13]. Male; age sixty-one. In July, 1897, erythromelalgia appeared in the fourth and fifth toes of the right foot, but, after three months, these became practically well, and the second and third toes were in turn attacked. These later greatly improved, and, at the time Dr. Mitchell saw the patient, about eight months after the original onset, the great toe was the seat of violent pain. It was impossible to feel any pulse in the right leg below the groin, and, on account of the general condition of the vascular system, it was decided to amputate only the right great toe. The nerves and arteries of the amputated part were carefully studied. The nerve bundles were composed almost entirely of connective tissue, and only a few undegenerated nerve fibers were seen. In most of the arteries there was considerable increase of the muscular tissue, and in all, even the smallest, there was great proliferation of the intima, so that in some vessels the lumen was almost obliterated. Increase of elastic tissue was also found. The walls of the veins were also thickened. The bones were enlarged.

The following is Auerbach's[4] case: Male; age forty-six; right foot and leg much affected by erythromelalgia, left slightly so; duration of disease, twenty-six years; tabes suspected. Had marked septic infection just previous to death. Forty-three hours afterward, permission was granted to remove the spinal cord, the posterior root ganglia and the nerves of the lower extremities. The microscopic examination was made by Professor Edinger, who, on account of the death from a septic condition and the delay in securing the post-mortem examination, found it impossible to make any positive assertion as to the value of the cell studies. The examination of the sciatic, tibial, peroneal and foot nerves resulted in wholly negative findings. There was thickening of the intima and media of the vessels, but it was equal on the two sides and not more than the age of the patient warranted. Seven posterior root ganglia from the lumbar and sacral nerves were taken, but in none of these was a single positive pathological condition found. There was a nuclear proliferation about the nerve fibers and the groups of nerve cells, but it was equal on the two sides and not considered of much importance. In the cauda equina almost half the nerve bundles on the right side and a few on the left side were wholly degenerated. They were spread over the entire field, but were much more numerous in the dorsal part of the section than elsewhere. In the lower part of the cord the posterior columns were much degenerated, except for a narrow wedge of normal nerve bundles directly next the posterior median fissure on both sides, and the degeneration was greatest on that side (right) on which the most degenerated fibers were seen in the cauda equina. The abnormal fibers entering the cord were gradually replaced by normal fibers until, at the level of the middle of the lumbar swelling, only a single degenerated bundle could be seen entering. In the thoracic and cervical cord, only the most median part of Goll's column was degenerated. No pathological changes in the cell columns were found.

Sachs'[6] case was as follows: Male; age thirty-six. His illness began in August, 1897, and he came under Dr. Sachs' care in April, 1898, with well-marked symptoms of erythromelalgia of the left foot and leg. Owing to the development of an ulcer on the dorsum of the foot, and later of gangrene of the toes, an amputation at the lower third of the thigh was performed October 31, 1898. Sections from the anterior tibial and popliteal arteries and from the anterior and posterior tibial, peroneal and sciatic nerves, along with some veins and some muscular tissue, were removed from the amputated leg for study. The sciatic and popliteal nerves were practically normal. The anterior tibial and peroneal were slightly degenerated. There was no peri-neuritis. All of the arteries were diseased; the anterior tibial and the popliteal and their branches, the most so. The arteritis was particularly noticeable where the vessel accompanied a nerve bundle, and, in many such, the lumen was occluded. All the coats were affected, but the intima particularly so, and, as there was here a considerable amount of new fibrous tissue, it is probable that the disease was of old standing. The veins showed a very slight thickening. The muscular tissue was normal.

In a consideration of these cases, one cannot but be impressed with the marked changes demonstrated in the vascular system and the relative infrequency of any definite lesions in the nervous system, either central or peripheral. In his early communications, Dr. Mitchell was of the opinion that the disease might be due to some central disturbance in the nervous system, but, in his more recent studies, he has been inclined to the view that it is dependent on a nerve-end neuritis. In the last paper[13] by Mitchell and Spiller—having in view Auerbach's case as well as their own—they say: "We must conclude that involvement of the sensory fibers anywhere between the spinal cord—or possibly within the spinal cord—and the peripheral ramifications is capable, under certain circumstances, of causing erythromelalgia." They believe that the symptoms in their own case were due to a peripheral neuritis. Auerbach[4] concludes that the phenomena may be of either central or peripheral nervous origin, while Lewin and Benda[19] divide all cases into three classes, viz.: (1) Those with true organic disease of the central nervous system; (2) those with functional disease of the central nervous system; (3) those with peripheral disease of the nervous system, either functional or organic. Dehio[9] believes that the essential lesion is in the posterior and lateral horns of the cord, and Collier[3] thinks that erythromelalgia is merely a symptom of organic disease of the spinal cord and "may be of great value in diagnosis."

Nearly all the early studies seem to have been undertaken with the idea that in the nervous system would be found the important pathological changes and, as Barlow[20] in his excellent article says, the inability to find clinical evidence of degeneration in the larger arteries seems to have still further drawn attention away from the vascular system. Thus Auerbach[4] in his report gives four cases from his own experience, all of which seem to have presented fairly typical signs of erythromelalgia, except that in the first two the disease progressed with unusual rapidity, and was associated with a considerable degree of arteriosclerosis. He thus concludes his report: "These cases (the first two) depending clearly upon an arteriosclerotic basis, should, in my judgment, be entirely separated from the nervous affection erythromelalgia." Why such cases should be excluded when the real nature of the disease has certainly so far not been established, it is difficult to understand.

Two recent writers have expressed views quite different from those given above. Savill[16] thinks the disease is due to a vasomotor paralysis dependent on a toxic condition of the blood, and considers that it is merely an advanced stage of acroparesthesia and may terminate in Raynaud's disease. Sachs,[6] in closing his interesting paper, says: "As a result of our studies, imperfect as they are, the questions put at the beginning of this paper may be answered thus: Erythromelalgia cannot be considered a *morbus sui generis;* it is a complex of symptoms which *may* be associated with diseases of central origin, but has been shown to be due to disease of the peripheral arteries. It cannot be denied that this obliterating endarteritis may be caused by central or peripheral nerve diseases, but the findings in one of our own cases render this unlikely, and comparison with conditions closely resembling erythromelalgia following upon marked cardiac and arterial disease leads to the inference that this symptom-group may be developed in the presence of arterial disease without any preceding nervous affection. Surely erythromelalgia is as much an arterial as a nerve disease."

Indeed, from a pathological standpoint, it would appear, in many cases, to be much more an arterial than a nervous disease. In Dehio's,[9] Elsner's,[7] and one of Mitchell's[10] cases, there was abundant evidence of arterial disease, but no degeneration of the nerves, and, in Auerbach's[4] case, the peripheral nerves were not affected. In Sachs'[6] case and my own the disease of the arteries was out of all proportion to the degeneration of the nerves, and the fact that, in my case, no such degeneration of the cord was present as was found by Auerbach and pointed out by Collier shows, at least, that this is not a necessary accompaniment of erythromelalgia.

Granting, however, that the arterial disease is the primary and most apparent lesion, and that the neuritis is secondary, it is still necessary to explain the arterial condition. It has been usual to speak of some disorder of the vasomotor system in order to account for the sudden flushing of the affected parts and, with this rather vague explanation, it seems we must be satisfied in the present state of our knowledge. The unilateral sweating in my case, probably of vasomotor origin, seems to lend support to this view. Before we can arrive at any positive conclusions as to the definite location of the essential lesion a more careful study must be made of the vascular system and of the entire nervous system, including the sympathetic ganglia. Judging from the collected anatomical studies and from my own material, I am inclined to consider the disease as much more nearly related to Friedländer's obliterative arteritis than to a degeneration of the spinal cord. Certainly the only marked, constant and general pathological changes in my case were found in the vascular system.

NOTE.—Since the preparation of the above report, my attention has been called to an article, by Dr. H. Batty Shaw, in the

British Medical Journal of March 21, 1903, presenting pathological findings in three amputated extremities in cases of erythromelalgia. A careful study of the nerves and vessels was made in each instance. In all there was considerable thickening of the intima of the vessels, but the degree varied in the different cases, and in different vessels in the same case. In case No. 1 the proliferation of the intima was greater in the veins than in the arteries. In all three the nerve fibers seemed normal. In conclusion the author says: "As a result of a consideration of these reported cases, it would appear that erythromelalgia, when occurring independently of central nervous change, is associated with but one morbid picture, that of local vascular change."

I have also, in this interval, become acquainted with another case of erythromelalgia—the individual having been a friend of the patient described above. He is now about seventy years of age and a lawyer by profession. About five and one-half years ago, he began to suffer from erythromelalgia in the right foot. The condition grew worse, and, after some months, appeared in the left foot also, but was never so severe there as in the right. He tried various physicians and methods of treatment without benefit, and, two and one-half years ago, consulted Dr. Dana, of New York, who kindly furnished me the following notes as to the patient's condition at that time.

The symptoms of erythromelalgia were well marked in both feet, but there was no disturbance of the reflexes, no evidence of anesthesia, no atrophy of the muscles, no arteriosclerosis and no indication of peripheral neuritis. The urine examination was negative, except for the presence of a trace of albumin. Iodide of mercury, large doses of salicylates and various local applications were tried without benefit, and Dr. Dana then recommended a resection of the sensory branches of the sciatic nerve in the right leg. The operation was performed by Dr. Jepson, of Sioux City, Iowa. For a time afterward there seems to have been some relief, but, at the end of six months, the patient says the pain was quite as severe as before. At that time, he applied to Dr. Albert Fensch, of Omaha, under whose care the treatment described below was carried out, and who furnished me the information concerning it.

The patient was then, on account of his pain, quite unable to get about without the assistance of an attendant. He was also having some trouble with an enlarged postate, but, aside from this and his erythromelalgia, his physical condition was quite good. He was first given glycero-phosphate of soda, hypodermically, for three weeks, with considerable improvement; but the drug which seemed to give most relief was aspirin.* He is now able to walk four miles or more each day, and has no pain whatever in the left foot and leg. His greatest complaint is that the right foot becomes very cold in winter and is not as much under his control as the left. He states also that it pains him slightly during stormy weather, but that aspirin usually easily controls this. There is but little in his condition at this time to make one think of erythromelalgia, but the fact that Dr. Dana considered it such, and that the diagnosis was concurred in by other eminent physicians, including Dr. Sachs, of New York, seems to place the diagnosis quite beyond dispute.

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*It is difficult for me to see how this treatment could have been of any avail in staying the pathological progress in my patient, even though it might have relieved his pain.

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